

6976-91349 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 10/762,616

Confirmation No.: 5023

Applicant: HERNANDEZ RAMIREZ et al.

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Docket No.: 6976-91349

Customer No.: 24628

Title: Title: ASSOCIATION OF FLUCONAZOLE-TINIDAZOLE FOR THE TREATMENT OF VAGINAL INFECTIONS, ITS COMPOSITION, PREPARATION PROCESS AND USAGE

DECLARATION OF LUISA HERNANDEZ-RAMIREZ

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Dear Sir:

1. I am Luisa Hernandez-Ramirez, identified above as inventor of above-identified patent application
2. I am an inventor of the invention described and claimed in the above –identified patent application.
3. I, therefore, am familiar with the subject matter described in the above-identified patent application.
4. I have conducted a study of 42 females over 18 years old, not pregnant, who showed signs of vaginal infections. This is the study set forth in the subject application pages 22-25.

5. The patients were divided into two groups; Group 1 was given one 150mg does of Fluconazole and a 2g tinidazole (standard dose). Group 2 was given a 112.5 mg Fluconazole 1500 mg tinidazole association.

6. The medication was given to both groups twice in one day.

7. Group 2 yielded surprising results.

8. All the patients submitted to a gynecological exploration in order to determine the characteristics of vaginal discharge and the accompanying symptoms were recorded. An initial and post treatment vaginal culture was conducted. The patients were asked to refrain from sexual intercourse in the interval between the taking of the vaginal cultures.

9. The initial symptoms evaluated were: odor, itching, vulva irritation, dysperunia and vaginal secretion, which decreased significantly after the treatment.

10. The results of the initial culture are shown in the following table:

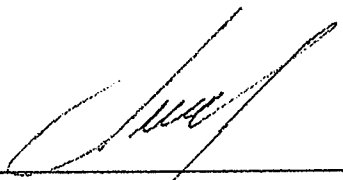
Infection	No of cases
Gardnerella Vaginalis	29
Gardnerella and Actinomyces	1
Gardnerella and Candida	3
Gardnerella and Micrococcus	1
Bacterial Vaginosis	2
B. Vaginosus and yeast	1
B. Vaginosis and Proteus	1
B. Vaginosis and micrococcus	1
B. Vaginosis and E. Coli	1
Trichomonas Vaqinalis	1
Trichomonas V.+Gardnerella+E. Coli	1
Total number of cases	2

11. The response to the treatment was as follows:

12. In Group 1 which was given the standard dose, microbiological eradication was 82%.

13. In Group 2 microbiological eradication was 80%.
14. Statistically there is no significant difference between Group 1 and Group 2.
15. As regards adverse effects, only one patient reported having sufferance dizziness and 3 complained from epigastralgia, all of which were temporary.
16. The adverse effects, significantly, were less in Group 2 than in Group 1, as shown in Exhibit A.
17. I conclude from the above described study that it is critical to lower the specific dosage given to a patient to less than 2000mg tinidazole and less than 150mg Fluconazole in the treatment of infection disease of the female reproductive system, in order to decrease the number of adverse reactions.
18. All statements made herein of my own knowledge are true and all statements made on information belief are believe to be true; and further, these statements were made with the knowledge that willful, false statement and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Date: 3 December 2008



Luisa Hernandez-Ramirez